K000006

FEB 28 2000

510 (k) Summary
Safety and Effectiveness

This summary of safety and effectiveness information has been prepared in accordance with the requirements of SMDA 1990 and 21 CFR Part 807.92.

Name: **Address:**	Diagnostic Products Corporation 5700 West 96th Street Los Angeles, CA 90045
Telephone Number: **Facsimile Number:**	(310) 645-8200 (310) 645-9999
Contact Person:	Edward M. Levine, Ph.D. Director of Clinical Affairs
Date of Preparation:	December 27, 1999
Device Name: Trade:	IMMULITE® Phenytoin IMMULITE® 2000 Phenytoin
Catalog Number:	LKPN1 (100 tests), LKPN5 (500 tests) L2KPN1 (200 tests), L2KPN6 (600 tests)
CFR:	A diphenylhydantoin test system is a device intended to measure diphenylhydantoin, an antiepileptic drug, in human specimens. Measurements obtained by this device are used in the diagnosis and treatment of diphenylhydantoin overdose and in monitoring levels of diphenylhydantoin to ensure appropriate therapy.
Common:	Reagent system for the determination of phenytoin in serum or heparinized plasma
Classification:	Class II device, 91-DIP (21 CFR 862.3350)
Panel:	Toxicology
CLIA Complexity Category:	We believe the category to be moderate, based on previous classification of analogous tests.
Manufacturer:	Diagnostic Products Corporation (DPC) 5700 West 96th Street Los Angeles, CA 90045-559

Establishment Registration #:	DPC's establishment Registration No. is 2017183
Substantially Equivalent Predicate Device:	Abbott AxSYM® Phenytoin (K935375) Dade ACA® Phenytoin (K843209)
Description of Device:	IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin are solid-phase, chemiluminescent enzyme immunoassays for use with their respective IMMULITE® and IMMULITE® 2000 Automated Analyzers.
Intended Use of the Device:	IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin are for *in vitro* diagnostic use for the quantitative measurement of phenytoin in serum or heparinized plasma, as an aid in monitoring drug therapy.

Technology:

This section does not contain any new information for a reviewer who is familiar with the DPC IMMULITE® System based upon the review of previous IMMULITE and IMMULITE 2000 assay submissions.

IMMULITE Phenytoin is a solid-phase, chemiluminescent immunoassay. The solid-phase, a polystyrene bead enclosed within a IMMULITE Test Unit, is coated with a polyclonal antibody specific for phenytoin.

The patient sample and alkaline phosphatase-conjugated phenytoin are simultaneously introduced into the Test Unit and incubated for approximately 30 minutes at 37 °C with intermittent agitation. During this time, phenytoin in the samples competes with enzyme-labeled phenytoin for a limited number of antibody binding sites on the bead. Unbound enzyme conjugate is then removed by a centrifugal wash, after which substrate is added and the Test Unit is incubated for a further 10 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is inversely proportional to the concentration of phenytoin in the sample.

IMMULITE 2000 Phenytoin is a solid-phase, chemiluminescent immunoassay. The solid-phase, polystyrene bead, is coated with a polyclonal antibody specific for phenytoin.

The patient sample and alkaline phosphatase-conjugated phenytoin acid are simultaneously introduced into the Reaction Tube and incubated for approximately 30 minutes at 37°C with intermittent agitation. During this time, phenytoin in the samples competes with enzyme-labeled phenytoin for a limited number of antibody binding sites on the bead. Unbound enzyme conjugate is then removed by a centrifugal wash, after which substrate is added and the Reaction Tube is incubated for an additional 5 minutes.

The chemiluminescent substrate, a phosphate ester of adamantyl dioxetane, undergoes hydrolysis in the presence of alkaline phosphatase to yield an unstable intermediate. The continuous production of this intermediate results in the sustained emission of light, thus improving precision by providing a window for multiple readings. The bound complex - and thus also the photon output, as measured by the luminometer - is inversely proportional to the concentration of phenytoin in the sample.

Abbott AxSYM Phenytoin utilizes fluorescence polarization immunoassay technology in a competitive ligand format. The unlabeled drug (antigen being measured) competes with the fluorescent-labeled antigen for the antibody binding sites. With increasing concentration of unlabeled antigen, more fluorescent-labeled antigen becomes unbound. Therefore, the fluorescent polarization signal decreases as the drug concentration increases, as measured by the fluorometer. Concentrations are determined from a stored standard curve.

Dade ACA Phenytoin uses matched lots of monoclonal phenytoin antibody and the phenytoin-glucose-6-phosphate dehydrogenase conjugate are used in this methodology. The concentration of phenytoin determines the amount of phenytoin-glucose-phosphate dehydrogenase conjugate that is bound to the phenytoin antibody. The unbound conjugate catalyzes the oxidation of glucose-6-phosphatase with the simultaneous reduction of NAD^+ to NADH more rapidly than does the bound conjugate. The rate of increasing absorbance at 340 nm due to the increase in NADH is related to phenytoin concentration by a mathematical function.

Performance Equivalence:

Diagnostic Products Corporation asserts that the IMMULITE Phenytoin and IMMULITE 2000 Phenytoin produce substantially equivalent results to other commercially marketed phenytoin assays, such as Abbott AxSYM Phenytoin or Dade ACA Phenytoin (used with the ACA® Star™ Analyzer). Each product is designed for the quantitative measurement of phenytoin in serum or heparinized plasma. Each product is intended strictly for in vitro diagnostic use as an aid in monitoring drug therapy.

Method Comparison:

The IMMULITE Phenytoin procedure was compared to a commercially available assay (Abbott AxSYM) on 95 patient samples, with phenytoin concentrations ranging from approximately 4.8 to 39 µg/mL. Linear regression analysis yielded the following statistics.

(IMMULITE) = 1.04 (Abbott) + 0.87 µg/mL r = 0.988

Means: 21.1 µg/mL (IMMULITE)
18.6 µg/mL (Abbott)

The IMMULITE 2000 Phenytoin procedure was compared to Dade ACA Phenytoin (using the ACA® Star™ Analyzer) on 51 samples, with phenytoin concentrations ranging from approximately 3.3 to 30 µg/mL. Linear regression yielded the following statistics.

(IML2000) = 0.94 (Dade) – 0.05 µg/mL r = 0.984

Means: 11.0 µg/mL (IMMULITE 2000)
11.7 µg/mL (Dade)

Conclusion:

The data presented in this summary of safety and effectiveness is the data that the Food and Drug Administration used in granting DPC substantial equivalence for IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin.

12/27/99

Edward M. Levine, Ph.D.
Director of Clinical Affairs

Date

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 28 2000

Edward M. Levine, Ph.D.
Director of Clinical Affairs
Diagnostic Products Corporation
5700 West 96th Street
Los Angeles, California 90045-5597

Re: K000006
Trade Name: IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin
Regulatory Class: II
Product Code: DIP
Dated: December 27, 1999
Received: January 3, 2000

Dear Dr. Levine:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known): K00 0006

Device Name: **IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin**

Indications For Use:

IMMULITE® Phenytoin and IMMULITE® 2000 Phenytoin are for *in vitro* diagnostic use with their respective IMMULITE and IMMULITE 2000 Analyzers - for the quantitative measurement of phenytoin in serum or heparinized plasma, as an aid in monitoring drug therapy.

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K000006

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

✓

Prescription Use
(Per 21 CFR 801.109)

OR

Over-The-Counter Use